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EXXON CHEMICAL COMPANY

EXXON CHEMICAL

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Safety and Environmental Affairs Department
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MANAGER, SAFETY PROGRAMS

January 29, 1998

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Attn: TSCA Section 8(e) Coordinator
Office of Pollution Prevention and Toxics
U. S. Environmental Protection Agency
401 M Street, S. W.
Washington, D. C. 20460-0001

88980000084

Contains No CBI

Re: Notification of Substantial Risk Under TSCA Section 8(e)

Dear Sir or Madam:

Under the provisions of Section 8(e) of the Toxic Substances Control Act, Exxon Chemical Company is submitting the following information describing the results of a recent toxicity study on Carbamodithioic acid, dimethyl-, sodium salt (CAS Registry Number 128-04-1). This chemical is also known by the common name Dimethyldithiocarbamic acid, sodium salt and is referred to in this notification as DMDTC. It us our understanding that this chemical is manufactured for commercial purposes by one or more companies in the United States. However, this chemical is not manufactured by Exxon Chemical Company and is used by us only for research and development purposes.

The study reported here was conducted to research the possible interaction of DMDTC with the metabolism and toxicity of 1,3-butadiene (CAS Registry Number 106-99-0). The study was conducted by Exxon Biomedical Sciences, Inc. The reason for this research is that it is our understanding that DMDTC is used commercially as a process chemical in the polymerization of 1,3-butadiene to form synthetic rubbers. In these manufacturing processes, workers may be simultaneously exposed to both 1,3-butadiene and DMDTC.

Although the study involved both DMDTC and 1,3-butadiene, this Section 8(e) notification is focused on a potential hazard associated only with exposure to DMDTC. No new hazards or risks associated with exposure to 1,3-butadiene were identified in this study. However, all of the results from this study, as well as results from follow-up research that is in progress, may be very relevant to understanding the toxicity and epidemiology of 1,3-butadiene under conditions of co-exposure to DMDTC. We plan to report all of these results as a FYI notification, with a discussion of their relevance, when additional research results are available in the near future.

Summary of Results

The study reported in this notification is a bone marrow micronucleus assay involving dermal exposure of DMDTC to $B_6C_3F_1$ mice. The DMDTC was purchased commercially as a solid dihydrate (empirical formula $C_3H_6NS_2Na \bullet 2H_2O$) with a stated purity of 98%. The mice were dermally exposed to DMDTC at a dose of 300 mg/kg (as an aqueous solution) either alone or with co-exposure to 1,3-butadiene at nominal inhalation concentrations of 10 and 200 ppm. Controls included mice exposed dermally to water only, mice exposed by inhalation to air only, and mice exposed by inhalation to 1,3-butadiene without dermal exposure to DMDTC. The experimental design for the study is provided in Table 1.

There was a statistically and biologically significant increase in blood reticulocytes (polychromatic erythrocytes (PCE's)) in all DMDTC dose groups, with and without 1,3-butadiene co-exposure, versus the test controls exposed to water or air only. In addition, there were statistically significant increases in bone marrow PCE's and spleen

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weight with exposure to DMDTC alone. These preliminary results indicate that DMDTC penetrated the mouse skin and produced effects on the bone marrow. Increased production of PCE's can be an indication that there has been a toxic injury to blood cells or the bone marrow and that a regenerative process is taking place. Details on the results are provided in the attached charts.

There is a large body of published literature on the genotoxicity of 1,3-butadiene, which was confirmed in this study. Thus, this notification is focused on DMDTC and no new hazards or risks associated with 1,3-butadiene are being reported. However, little has been published on the toxicology of DMDTC and the results reported here may be useful to others for hazard identification purposes.

Literature on a similar chemical, Methyldithiocarbamic acid, sodium salt, showed an increased production of bone marrow cells and immunological alterations following oral exposure in this same strain of mice. Immunological alterations and increased spleen weights were also observed in mice exposed by the dermal route in those studies (bone marrow cellularity was not examined). However, the data was not from a genotoxicity study and different endpoints were measured.

A formal report on the results reported here has not been issued at this time. At such time when a report is available, we will provide a copy to EPA as a follow-up to this notification. If you have any questions or need additional information, please feel free to contact me on (281) 870-6874.

Sincerely yours,

Steven G. Hentges

SGH/jad
Attachments

IN VIVO MAMMALIAN MICRONUCLEUS ASSAY - DERMAL AND INHALATION EXPOSURE
Dimethyldithiocabamic acid, sodium salt and 1,3-Butadiene

TABLE 1

EXPERIMENTAL GROUPS

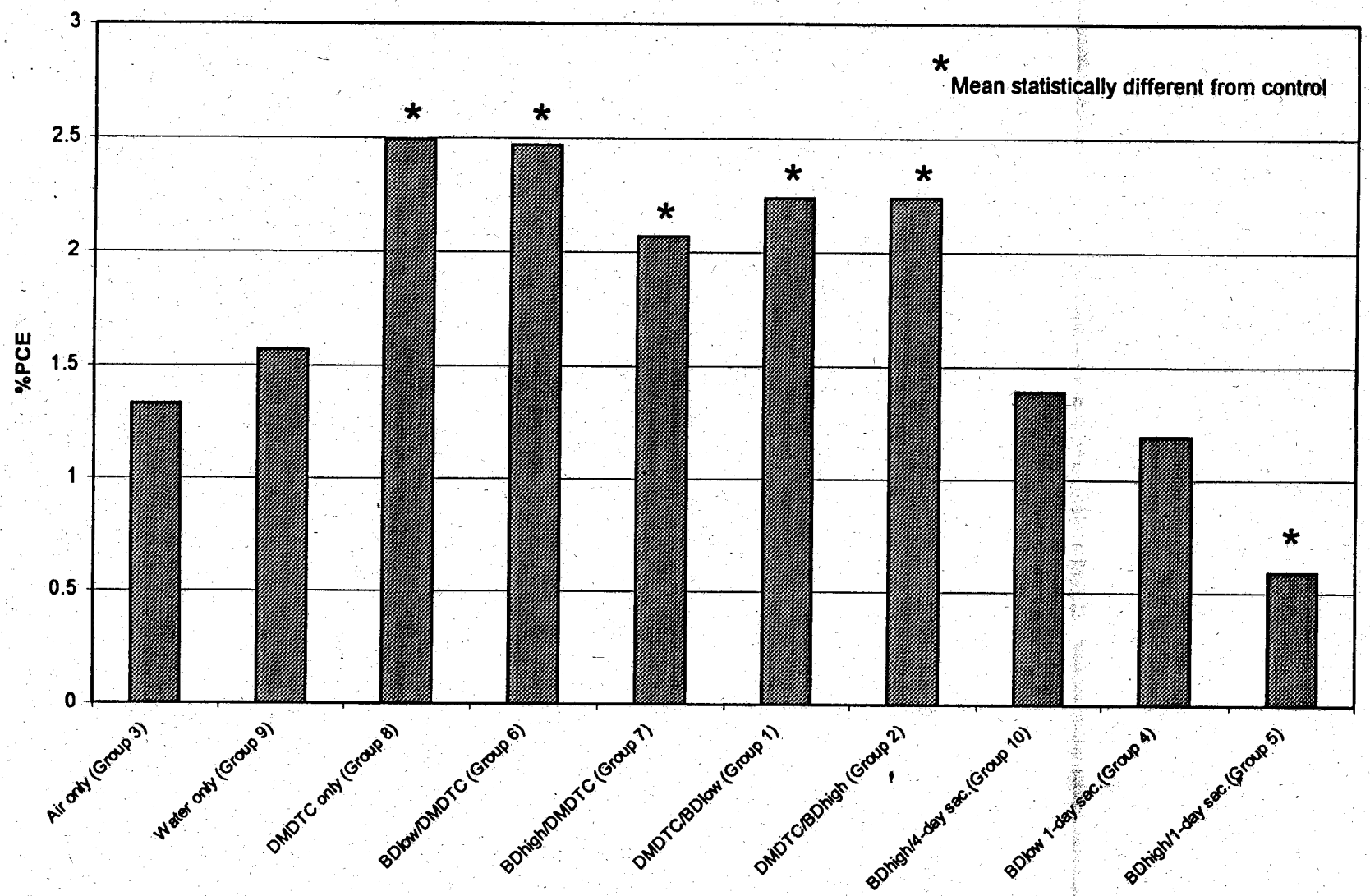
Group[e]	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9
1	DMDTC[a]	DMDTC	DMDTC	DMDTC +BD low[b]	BD low	Sacrifice			
2	DMDTC	DMDTC	DMDTC	DMDTC + BD / high[c]	BD high	Sacrifice			
3				Air	Air	Sacrifice			
4				BD Low	BD Low	Sacrifice			
5[d]				BD high	BD high	Sacrifice			
6				BD low	BD low +DMDTC	DMDTC	DMDTC	DMDTC	Sacrifice
7				BD high	BD high +DMDTC	DMDTC	DMDTC	DMDTC	Sacrifice
8					DMDTC	DMDTC	DMDTC	DMDTC	Sacrifice
9					Water	Water	Water	Water	Sacrifice
10				BD high	BD high				Sacrifice

a Dimethyldithiocabamic acid, sodium salt - 300 mg/kg
b 1,3-butadiene - 10ppm
c 1,3-butadiene - 200ppm
d Designated as the positive control for the study
e 5 male and 5 female B6C3F1 mice per dose

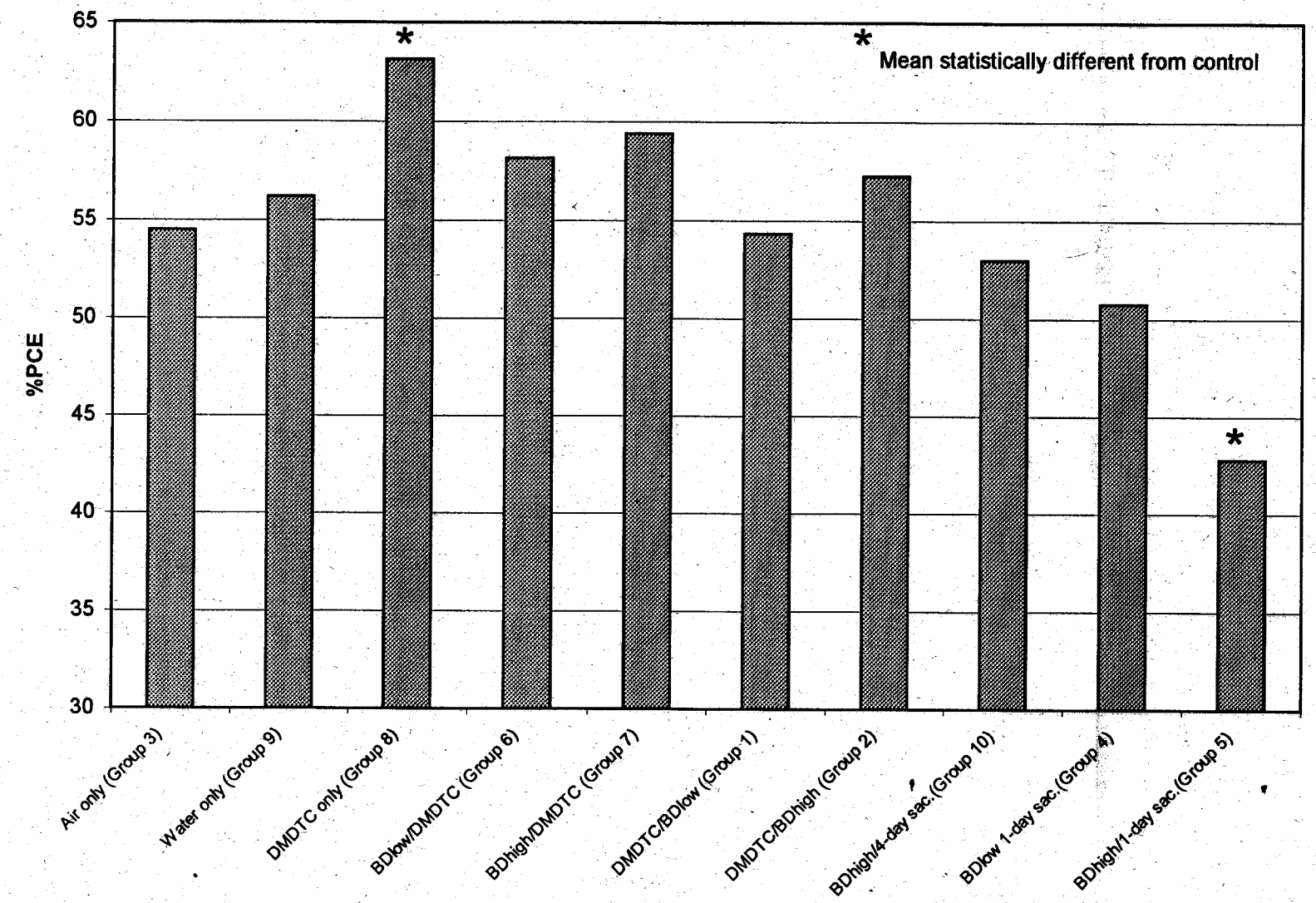
Immediately prior to dosing, acetone was applied to the shaved upper dorsal region of mice from groups 1, 2, 6, 7, 8, and 9.

Group	%MN-bone	%MN-blood	%PCE-bone	%PCE-blood
Air only (Group 3)	0.2	0.22	54.5	1.33
Water only (Group 9)	0.11	0.18	56.2	1.57
DMDTC only (Group 8)	0.12	0.16	63.15	2.49
BDlow/DMDTC (Group 6)	0.22	0.15	58.15	2.47
BDhigh/DMDTC (Group 7)	0.14	0.24	59.4	2.07
DMDTC/BDlow (Group 1)	0.19	0.17	54.32	2.24
DMDTC/BDhigh (Group 2)	0.68	0.19	57.25	2.24
BDhigh/4-day sac.(Group 10)	0.26	0.2	53	1.39
BDlow 1-day sac.(Group 4)	0.44	0.42	50.75	1.19
BDhigh/1-day sac.(Group 5)	1.66	1.66	42.8	0.59

Study 112530: %PCE-Blood



Study 112530: %PCE-Bone Marrow



Study 112530: %MN - Bone Marrow and Blood